

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 10:46:19 ON 24 JAN 2005

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 JAN 2005 HIGHEST RN 819046-01-0

DICTIONARY FILE UPDATES: 23 JAN 2005 HIGHEST RN 819046-01-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

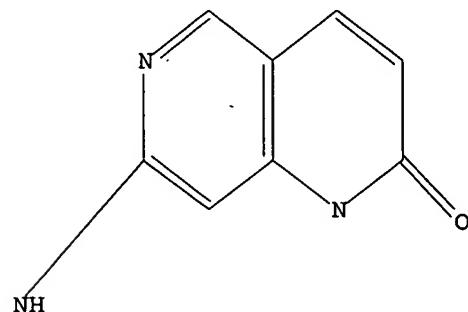
Uploading C:\Program Files\Stnexp\Queries\ppgg.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 10:46:51 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2415 TO ITERATE

41.4% PROCESSED 1000 ITERATIONS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

9 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 45353 TO 51247
PROJECTED ANSWERS: 155 TO 713

L2 9 SEA SSS SAM L1

=> file caplus
COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 0.43 | 0.64 |

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 10:47:02 ON 24 JAN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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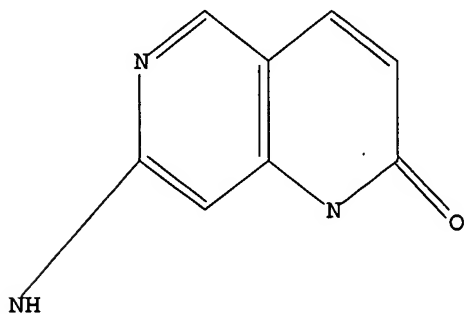
FILE COVERS 1907 - 24 Jan 2005 VOL 142 ISS 5
FILE LAST UPDATED: 23 Jan 2005 (20050123/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 10:48:57 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2415 TO ITERATE

41.4% PROCESSED 1000 ITERATIONS 9 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 45353 TO 51247
PROJECTED ANSWERS: 155 TO 713

L3 9 SEA SSS SAM L1

L4 2 L3

=> d l4 ibib abs hitstr 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:473076 CAPLUS

DOCUMENT NUMBER: 133:252336

TITLE: Synthesis and Structure-Activity Relationships of
7-Substituted 3-(2,6-Dichlorophenyl)-1,6-naphthyridin-
2(1H)-ones as Selective Inhibitors of pp60c-src
AUTHOR(S): Thompson, Andrew M.; Rewcastle, Gordon W.; Boushelle,
Stacey L.; Hartl, Brian G.; Kraker, Alan J.; Lu, Gina
H.; Batley, Brian L.; Panek, Robert L.; Showalter, H.
D. Hollis; Denny, William A.

CORPORATE SOURCE: Auckland Cancer Society Research Centre Faculty of
Medical and Health Sciences, University of Auckland,
Auckland, 92019, N. Z.

SOURCE: Journal of Medicinal Chemistry (2000), 43(16),
3134-3147

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 7-Substituted 3-(2,6-dichlorophenyl)-1,6-naphthyridin-2(1H)-ones are
potent inhibitors of protein tyrosine kinases, with some selectivity for
c-Src. The compds. were prepared by condensing 4,6-diaminonicotinaldehyde
with 2,6-dichlorophenylacetonitrile and selectively converting the 2- and
7-amino groups of the product to hydroxy and fluoro groups, resp., by
prolonged diazotization in 50% aqueous fluoroboric acid. N-Methylation,
followed by treatment with aliphatic diamines, aromatic amines, or their
derived

lithium anions, gave the desired compds. Selected isomeric
1,8-naphthyridin-2(1H)-ones were also prepared in order to evaluate the
relative contributions of both ring A aza atoms of the related
pyrido[2,3-d]pyrimidin-7(8H)-ones to the inhibitory activity. The compds.
were evaluated for their ability to prevent phosphorylation of a model
substrate by c-Src, FGF-1 receptor, and PDGF- β receptor enzymes.
Overall, there was a high degree of correlation of the activities against
the different kinases, with c-Src being generally the most sensitive to

structural changes. 1,6-Naphthyridin-2(1H)-one analogs bearing basic aliphatic side chains [7-NH(CH₂)_nNRR, 7-NHC₆H₄O(CH₂)_nNRR, or 7-NHC₆H₄N(CH₂)₄NMe] were the most potent against c-Src (IC₅₀s of 10-80 nM), showing good selectivity with respect to PDGFR (10-300-fold) but less with respect to FGFR. The 1,6-naphthyridin-2(1H)-ones showed broadly similar activity to the analogous pyrido[2,3-d]pyrimidin-7(8H)-ones, whereas the 1,8-naphthyridin-2(1H)-ones were at least 103-fold less potent. These results, indicating that the 3-aza atom in the pyrido[2,3-d]pyrimidin-7(8H)-ones is mandatory, whereas the 1-aza atom is not, support the published binding model for these compds. to c-Src (J. Med. Chemical 1998, 41, 1752), where the 3-aza and 2-NH atoms form a bidentate H-bond donor-acceptor motif that interacts with Met341 and the 1-aza atom is not involved in specific binding interactions.

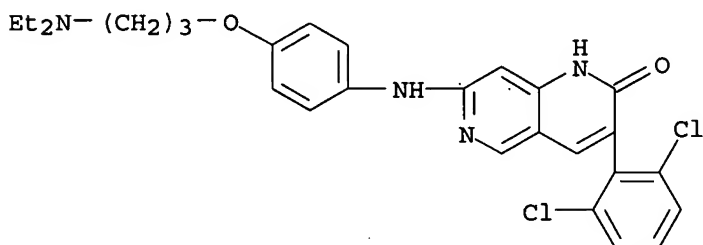
IT 294659-62-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and structure-activity relationships of 7-substituted 3-(2,6-Dichlorophenyl)-1,6-naphthyridin-2(1H)-ones as selective inhibitors of pp60c-src)

RN 294659-62-4 CAPLUS

CN 1,6-Naphthyridin-2(1H)-one, 3-(2,6-dichlorophenyl)-7-[[4-[3-(diethylamino)propoxy]phenyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:139846 CAPLUS

DOCUMENT NUMBER: 130:196643

TITLE: Preparation of naphthyridinones as protein tyrosine kinase and cyclin dependant kinase inhibitors

INVENTOR(S): Barvian, Mark Robert; Denny, William Alexander; Dobrusin, Ellen Myra; Hamby, James Marino; Showalter, Howard Daniel Hollis; Thompson, Andrew Mark; Winters, Roy Thomas; Wu, Zhipei

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 133 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9909030 | A1 | 19990225 | WO 1998-US16848 | 19980813 |
| W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, | | | | |

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|------------|----|----------|----------------|----------|
| AU 9888289 | A1 | 19990308 | AU 1998-88289 | 19980813 |
| AU 742999 | B2 | 20020117 | | |
| EP 1003745 | A1 | 20000531 | EP 1998-939941 | 19980813 |
| EP 1003745 | B1 | 20041229 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

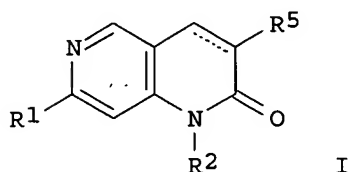
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|---------------|----|----------|----------------|----------|
| BR 9811956 | A | 20000815 | BR 1998-11956 | 19980813 |
| JP 2001515078 | T2 | 20010918 | JP 2000-509710 | 19980813 |
| NZ 502704 | A | 20020628 | NZ 1998-502704 | 19980813 |
| ZA 9807491 | A | 19990421 | ZA 1998-7491 | 19980819 |
| MX 9911792 | A | 20000630 | MX 1999-11792 | 19991215 |
| US 6150359 | A | 20001121 | US 2000-463553 | 20000126 |

PRIORITY APPLN. INFO.:

| | | |
|-----------------|---|----------|
| US 1997-56746P | P | 19970820 |
| WO 1998-US16848 | W | 19980813 |

OTHER SOURCE(S): MARPAT 130:196643

GI



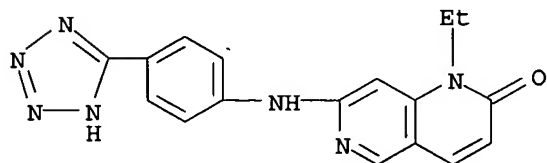
AB Title compds. [I; R1 = halo or (un)substituted amino; R2 = (bi)(cyclo)alkyl; R5 = H, halo, (hetero)aryl, etc.; dashed line = optional bond] were prepared Thus, 4,6-diamino-3-pyridinecarboxaldehyde (preparation given) was cyclocondensed with 2,6-Cl2C6H3CH2CN and the major product treated with NaNO2/HBF4 to give, after N-methylation, major product I (R2 = Me, R5 = C6H3Cl2-2,6) (II; R1 = F) which was aminated to give II (R1 = e.g., NHMe). Data for biol. activity of I were given.

IT 220817-54-9P 220817-74-3P 220818-88-2P
220818-94-0P 220819-14-7P 220819-55-6P
220820-58-6P 220821-14-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naphthyridinones as protein tyrosine kinase and cyclin dependant kinase inhibitors)

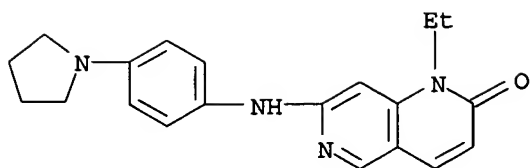
RN 220817-54-9 CAPLUS

CN 1,6-Naphthyridin-2(1H)-one, 1-ethyl-7-[[4-(1H-tetrazol-5-yl)phenyl]amino]-
(9CI) (CA INDEX NAME)



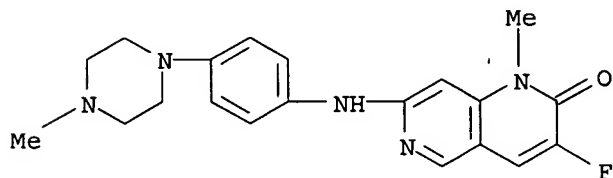
RN 220817-74-3 CAPLUS

CN 1,6-Naphthyridin-2(1H)-one, 1-ethyl-7-[[4-(1-pyrrolidinyl)phenyl]amino]-
(9CI) (CA INDEX NAME)



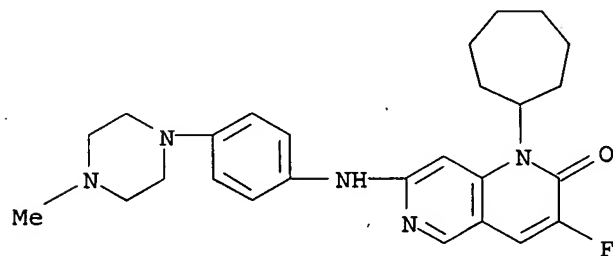
RN 220818-88-2 CAPLUS

CN 1,6-Naphthyridin-2(1H)-one, 3-fluoro-1-methyl-7-[[4-(4-methyl-1-piperazinyl)phenyl]amino]- (9CI) (CA INDEX NAME)



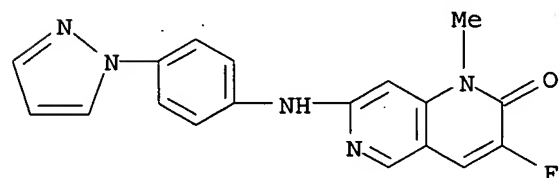
RN 220818-94-0 CAPLUS

CN 1,6-Naphthyridin-2(1H)-one, 1-cycloheptyl-3-fluoro-7-[[4-(4-methyl-1-piperazinyl)phenyl]amino]- (9CI) (CA INDEX NAME)



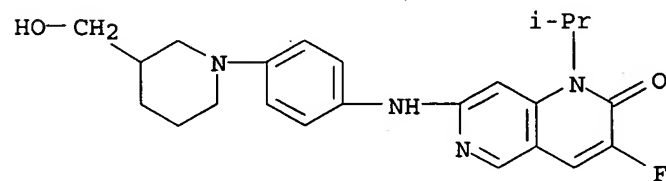
RN 220819-14-7 CAPLUS

CN 1,6-Naphthyridin-2(1H)-one, 3-fluoro-1-methyl-7-[[4-(1H-pyrazol-1-yl)phenyl]amino]- (9CI) (CA INDEX NAME)



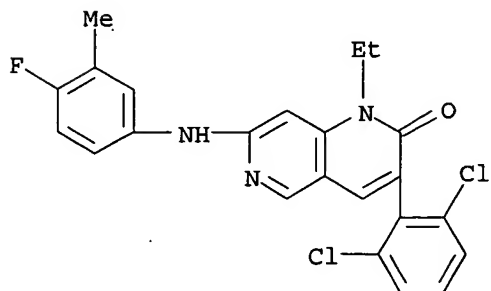
RN 220819-55-6 CAPLUS

CN 1,6-Naphthyridin-2(1H)-one, 3-fluoro-7-[[4-[3-(hydroxymethyl)-1-piperidinyl]phenyl]amino]-1-(1-methylethyl)- (9CI) (CA INDEX NAME)



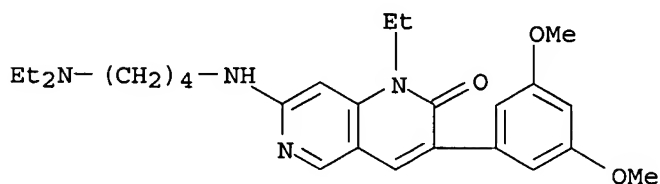
RN 220820-58-6 CAPLUS

• CN 1,6-Naphthyridin-2(1H)-one, 3-(2,6-dichlorophenyl)-1-ethyl-7-[(4-fluoro-3-methylphenyl)amino]- (9CI) (CA INDEX NAME)



RN 220821-14-7 CAPLUS

CN 1,6-Naphthyridin-2(1H)-one, 7-[[4-(diethylamino)butyl]amino]-3-(3,5-dimethoxyphenyl)-1-ethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

1

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT